REMARKS

Status of the Claims

Claims 34-35 are canceled without prejudice or disclaimer, and claims 24-25 and 28 are currently amended. No new matter has been added. Upon entry of this Amendment, claims 1, 6-7, 9-10, 14, 16-17, 19-33, and 36-45 are pending, and elected claims 24-33 and 36-45 should be examined. Applicants will request rejoinder of claims 1, 6-7, 9-10, 14, 16-17, and 19-23 with the elected claims when the elected claims are allowed.

Claim Objections

Claims 24-25 and 28 are objected to because they allegedly "recite improper uses of a period." See Office Action of January 29, 2003, page 2. Applicants believe the present version of the claims avoids this issue. Accordingly, the objection should be withdrawn.

Rejections- 35 U.S.C. § 101

Claims 24-33 and 36-45 were rejected under 35 U.S.C. § 101 for allegedly lacking a specific, substantial, and credible utility, or alternatively, a well-established utility. Office Action, page 3. Applicants respectfully traverse this rejection.

According to the PTO, the claimed invention is allegedly not supported by a substantial utility, "because no substantial utility has been adequately established." Office Action, page 3. Specifically, the PTO alleges " SEQ ID NO: 702, 6223, 10847, and 10848 may be involved in the asserted protein functions, such as those described in pages 216-241, but the mere fact that these are only asserted functions supports the notions that further research would be required to confirm a 'real world' context of use." Office Action, page 3.

According to the MPEP, "an assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a 'real world' context of use in identifying potential candidates for preventive measures or further monitoring." MPEP § 2107.01. Moreover, the MPEP states that in a situation where applicant discloses a specific biological activity and reasonably correlates that

activity to a disease condition, such a situation is sufficient to identify a specific utility for the invention. MPEP § 2107.01.

Such is the case here. For example, the specification teaches that SEQ ID NO: 706 and SEQ ID NO: 6223 of the elected claims have a specific utility, i.e., a utility specific to SEQ ID NO: 706 and SEQ ID NO: 6223. Both SEQ ID NO: 706 and SEQ ID NO: 6223 are described as associated with diabetes. Specifically, according to the specification, the expression level of HEMBA1004850, a clone containing SEQ ID NO: 706 and SEQ ID NO: 6223, was elevated in endothelial cells in a glycated protein specific manner (see p. 420, lines 30-42, and p. 632, line 9 of Table 169). As further disclosed in the specification on page 407, line 21, a non-enzymatic protein glycation reaction is believed to cause of a variety of chronic diabetic complications. Schmidt AM et al., *J Clin Invest.* Sep. 96(3):1395-403 (1995) (reporting a gene whose expression is significantly elevated or decreased in a glycated protein-specific manner in an endothelial cell and is associated with a diabetic complication caused by a glycated protein) (previously submitted). HEMBA1004850 contains such a gene and both SEQ ID NO: 706 and SEQ ID NO: 6223. Therefore, the specification states that both SEQ ID NO: 706 and SEQ ID NO: 6223 find a specific utility in the diagnosis and treatment of diabetes.

Contrary to the PTO's position, the as-filed specification not only discloses that elected clone HEMBA1004850 is associated with diabetes, but the specification also indicates that elevated HEMBA1004850 expression was observed in human pulmonary arterial cells cultured in medium containing glycosylated bovine serum albumin or an advanced glycosylated end product thereof, compared with control bovine serum albumin. Accordingly, HEMBA1004850 expression correlates with protein glycosylation, a complication associated with diabetes. Moreover, the specification discloses "vascular endothelial cells are affected with glycated proteins present in blood." See specification, page 407, lines 24-25. Clearly, it is useful to determine whether or not vascular endothelial cells have been exposed to glycated proteins. Since HEMBA1004850 expression increases when endothelial cells are exposed to glycated proteins, HEMBA1004850 provides a useful

diagnostic marker for assaying cell exposure to such glycated proteins.

Applying the standards of MPEP § 2107.01, the present invention finds a "real world" use, because it provides a means for determining (e.g. assaying) whether or not vascular endothelial cells have been exposed to glycated proteins, a useful thing to know. That is, since HEMBA 1004850 expression level is elevated when endothelial cells are contacted with glycated proteins, HEMBA1004850 is a useful diagnostic marker for indicating exposure of cells to such glycated proteins.

As the present invention finds a specific, substantial, and credible utility, or alternatively, a well-established utility, the rejection is improper and should be withdrawn.

Rejections- 35 U.S.C. § 112, first paragraph (Enablement)

Claims 24-33 and 36-45 were rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. In short, the PTO asserted that the claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility, and therefore one skilled in the art would not know how to use the claimed invention. Office Action, page 7. Applicants respectfully traverse this rejection.

As previously discussed, the subject matter embraced by the elected claims and sequences find specific, substantial, and credible utility. This issue has been addressed in the previous section and need not be repeated here. In light of the disclosed utility, however, Applicants respectfully submit that one skilled in the art, guided by the present specification's teachings, would readily know how to make and use the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejections- 35 U.S.C. § 112, first paragraph (written description)

There are two sets of rejections, each of which is addressed under separate headers.

A. Claims 28, 34-35, 37, 39, 41, 43, and 55 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of written description. Claim 28, and its dependent claims 34-35,

37, 39, 41, 43, and 45, are rejected on the grounds that the language "secretory or membrane protein associated with diabetes" allegedly does not find support in the as-filed specification. Office Action, page 8. As the present version of the claims avoids this issue, the rejection should be withdrawn.

B. Claims 24-33 and 36-45 were rejected on the grounds that the claims "encompass fragments and oligonucleotide (claims 24, 25, 34) as well as recited percentages of identity (claim 28) and hybridization to sequences (claim 28) which do not meet the written description provision of 35 U.S.C. § 112, first paragraph." Office Action, pages 8-10. As there are 12 grounds for rejection, each one is addressed as enumerated below.

1. Claims 24 and 34 (canceled) were rejected for reciting "fragment of the nucleotide sequence." Office Action, page 9. The present version of claim 24 provides specific structural support for the claimed primer set. While the specification discloses that any nucleotide sequence selected from the 5' and 3' untranslated region (UTR) of SEQ ID NO: 702 can be used for synthesizing full-length HEMBA1004850, the SEQ ID NO: 702 open reading frame (ORF) starts at position 415. See Specification, page 128, lines 16-18. To obtain the full length coding sequence of HEMBA1004850, the 5'-end nucleotide sequence should be selected from the 5'-end to the first ATG (position 415) of SEQ ID NO: 702. Therefore, one of ordinary skill in the art would recognize that nucleotide fragments comprising a nucleotide sequence selected from position 1-429 of the nucleotide sequence set forth in SEQ ID NO: 702 are useful for synthesizing the full coding region of HEMBA1004850. As the present version of the claim avoids this issues raised by the Examiner, the rejection should be withdrawn.

2. Claim 26 was rejected for reciting "the primer set." Office Action, page 9. As described above, the specification discloses that any nucleotide sequence selected from the 5' and 3' untranslated region (UTR) of SEQ ID NO: 702 can be used for synthesizing full-length HEMBA1004850. As the sequence set forth in SEQ ID NO: 702 has an open reading frame (ORF) starting at position 415, one of ordinary skill in the art would recognize that nucleotide fragments comprising a nucleotide sequence selected from position 1-429 of the nucleotide

sequence set forth in SEQ ID NO: 702 are useful for synthesizing the full coding region of HEMBA1004850.

Likewise, for obtaining the full length coding sequence of HEMBA1004850, the 3'-end nucleotide sequence should be selected from the 3'-UTR of SEQ ID NO: 10847. The 3'-UTR of SEQ ID NO: 10847 corresponds with positions 1-487 of SEQ ID NO: 6223. Therefore, one of ordinary skill in the art would recognize that nucleotide fragments comprising a nucleotide sequence selected from position 1-487 of the nucleotide sequence set forth in SEQ ID NO: 6223 are useful for synthesizing the full coding region of HEMBA1004850. As the present version of the claim avoids this issues raised by the Examiner, the rejection should be withdrawn.

3. Claim 27 was rejected for reciting "the coding region of the polynucleotide." Office Action, page 9. As the present version of the claims avoids this issue, the rejection should be withdrawn.

4. Claim 28 was rejected for reciting "comprising a coding region of the nucleotide sequence." Office Action, page 9. As the present version of the claim avoids this issue, the rejection should be withdrawn.

5. Claim 28 was rejected for reciting "comprising a nucleotide sequence encoding a protein comprising the amino acid sequence." Office Action, page 9. As the present version of the claim avoids this issue, the rejection should be withdrawn.

6. Claim 28 was rejected for reciting "the amino acid sequences." Office Action , page 9. As the present version of the claim avoids this issue, the rejection should be withdrawn.

7. Claim 28 was rejected for reciting "up to 5 % of the amino acids are substituted, deleted, inserted, and/or added." Office Action, page 9. As the present version of the claim avoids this issue, the rejection should be withdrawn.

8. Claim 28 was rejected for reciting "the nucleotide sequence." Office Action, page 9. As the present version of the claim avoids this issue, the rejection should be withdrawn.

9. Claim 28 was rejected for reciting "comprises a nucleotide sequence encoding a protein comprising a secretory or membrane protein associated with diabetes." Office Action, page 9. As the present version of the claim avoids this issue, the rejection should be withdrawn.

10. Claims 35-39 and 42-43 were rejected for reciting "the polynucleotide." Office Action, page 9. As the present version of the claim avoids this issue, the rejection should be withdrawn.

11. Claims 40-41 and 44-45 were rejected for reciting "the vector." Office Action, page 9. As the present version of the claim avoids this issue, the rejection should be withdrawn.

12. Claim 28 was rejected for reciting "95 % identity." Office Action, page 9. As the present version of the claim avoids this issue, the rejection should be withdrawn.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections.

Rejections- 35 U.S.C. § 112, second paragraph

Claims 28, 34, 37, 39, and 43 are rejected under 35 U.S.C. § 112, second paragraph for alleged indefiniteness. Specifically, the PTO maintains that the phrase "associated with diabetes" is allegedly unclear. Office Action, page 11. The present version of the claims avoids this issue. Accordingly, the rejection should be withdrawn.

Rejections-35 U.S.C. § 102(e)

Claims 28, 34-35, 37, 39, 41, 43, and 45 were rejected under 35 U.S.C. § 102(e)(2) as allegedly anticipated by Shin et al. (USPN 6,291,645). According to the PTO, Shin et al.

discloses "a 22-mer which matches residues 767-788 of SEQ ID NO: 10847," thereby allegedly anticipating the rejected claims.

A disclosure can not anticipate a claim, if the disclosure differs from the claimed invention. MPEP § 2131. Here, even if the PTO were correct, the cited 22-mer would still differ from the coding region of the full-length nucleotide sequence set forth in SEQ ID NO: 10847 or 10848. In other words, the cited passage does not anticipate the rejected claims. Accordingly, the rejection is improper and should be withdrawn.

CONCLUSION

As the above-presented amendments and remarks address and avoid each rejection presented by the Examiner, withdrawal of rejections and allowance of the claims are respectfully requested. No new matter has been added.

Applicants respectfully request that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing the claims in condition for allowance. Applicants submit that the proposed claim amendments neither raise new issues nor necessitate the undertaking of any additional search of the art by the Examiner, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner.

Finally, Applicants submit that the entry of the amendment would place the application in better form for appeal.

If there are any questions concerning this application, the Examiner is courteously invited to contact the undersigned counsel.

Respectfully submitted,

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